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<b>(21) International Application Number:</b> PCT/US92/10500 <b>(22) International Filing Date:</b> 7 December 1992 (07.12.92)  <b>(30) Priority data:</b> 805,432 11 December 1991 (11.12.91) US  <b>(71) Applicant:</b> THE PROCTER & GAMBLE COMPANY [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US).  <b>(72) Inventors:</b> HUNTER, Mary, Ann ; 8368 Jadwin Street, Cincinnati, OH 45216 (US). STAPLER, Judith, Hill ; 1084 Brown Road, Wilmington, OH 45177 (US).  <b>(74) Agents:</b> REED, David, T. et al.; The Procter & Gamble Company, 5299 Spring Grove Avenue, Cincinnati, OH 45202 (US).		<b>(81) Designated States:</b> CA, FI, NO, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> CETYLPYRIDINIUM CHLORIDE AND DOMIPHEN BROMIDE IN ORGANIC SOLVENT  <b>(57) Abstract</b>  The present invention relates to oral compositions in the form of microcapsules which reduce oral bacteria and provide long lasting breath protection.		

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CETYLPIRIDINIUM CHLORIDE AND DOMIPHEN  
BROMIDE IN ORGANIC SOLVENT

TECHNICAL FIELD

5           The present invention relates to oral compositions in the form of microcapsules which reduce oral bacteria and provide long lasting breath protection.

BACKGROUND OF THE INVENTION

10           The use of breath control compositions such as breath mints, mouthwashes, chewing gums, etc. is widespread in most of the developed countries of the world. Another form which has been used are microcapsules containing a flavorant or other breath protection agent. These executions have acceptance due not only to their usefulness away from a place to expectorate mouthwashes but also due to the fact that they can be swallowed when the user  
15           does not need any more of the actives or doesn't want the microcapsule in the mouth any longer.

20           Although microcapsules have been used, there are problems associated with incorporating certain breath protection agents/ antimicrobials into the core. Oftentimes the wall of the microcapsule may develop imperfections and cause loss of the contents prematurely. Additionally, the actives may not be easily solubilized in the materials usually present in the core.

25           The prior art discloses a variety of means for providing breath protection and reducing oral bacteria. Included among such means are sprays disclosed in U.S. 3,431,208, March 4, 1969 to Bailey. Particles containing an adhesive member are disclosed in U.S. 3,911,099, October 7, 1975 to Den Foney et al. Another form is a mouthwash concentrate in a unit dosage cup as disclosed in  
30           U.S. 4,312,889, January 26, 1982 to Melsheimer. All of these references are incorporated herein by reference.

35           The present inventors have found that by incorporating the breath control/antimicrobial actives into the core of the microcapsule along with organic diluents, problems associated with other microcapsule executions can be avoided.

It is therefore an object of the present invention to provide improved microcapsules.

It is another object of the present invention to provide microcapsules which provide improved breath control and reduce oral bacteria.

It is still another object of the present invention to provide improved methods of providing breath control and reducing oral bacteria.

These and other objects will become more apparent from the detailed description which follows.

All percentages and ratios used herein are by weight unless otherwise specified. Additionally, all measurements are made at 25°C unless otherwise specified.

#### SUMMARY OF THE INVENTION

The present invention in one of its aspects relates to microcapsules which contain breath control actives/antimicrobials in the core of the microcapsule along with an organic diluent.

#### DETAILED DESCRIPTION OF THE INVENTION

The essential as well as optional components of the capsules of the present invention are described in the following paragraphs.

##### Capsule Shell Material:

The shell material of the microcapsules of the present invention can be any materials which are suitable for ingestion as well as retention in the oral cavity. Materials which are suitable include gelatin, polyvinyl alcohols, waxes, gums and sugar candy type materials used in cough drops and mints, for example.

The shell material is used to form any of a wide variety of shapes such as spheres, oblong shapes, disks, puffed squares and cylinders. The shell thickness is preferably in the range of about 30um to about 2mm, preferably from about 70um to about 110um. If the microcapsules are spherical, the particle diameter is generally in the range of from about 2mm to about 9mm, preferably from about 3mm to about 7mm.

Breath Control Agents/Antimicrobials Present in the Core:

The breath control agents used in the cores of the microcapsules include quaternary ammonium salts such as pyridinium salts (e.g., cetyl pyridinium chloride), domiphen bromide, other cationic materials such as chlorhexidine salts, zinc salts and copper salts. Other organic agents such as triclosan and other noncationic water insoluble agents are also useful herein. Such materials are disclosed in U.S. Patent 5,043,154, August 27, 1991, incorporated by reference herein.

These breath control/antimicrobial agents are used in an amount of from about 0.001% to about 2%, preferably from about 0.005% to about 1% of the total core contents.

Diluents for Use in Microcapsule Core:

The solubilizing agent for the breath control/antimicrobial agents used in the cores of the present microcapsules can be any of a number of materials. Preferred are oils such as corn, olive, rapeseed, sesame, peanut or sunflower. Other preferred materials are triglycerides such as Captex 300. These are used in an amount of from about 20% to about 80%, preferably from about 65% to about 70% of the total capsule weight.

Additional Agents Suitable for Use in the Core of Capsule:

The core of the microcapsules of this invention may contain any number of additional materials to provide additional efficacy and/or sensory perceptions. Such agents may include flavoring agents such as thymol, eucalyptol, menthol, methyl salicylate or witch hazel. These agents are used in an amount of from about .1% to about 25%, preferably from about 10% to about 15% of the total capsule weight.

In addition, a variety of sweetening agents such as sugars, corn syrups, saccharin or aspartame may also be included in the core. These agents are used in an amount of from about .1% to about 5%, preferably from about .35% to about .5% of the total capsule weight.

Method of Manufacture:

The capsules of the present invention can be made using a variety of techniques. One method is described after the following examples.

Industrial Applicability:

The capsules of the present invention are used by placing the capsules into the mouth and retaining them therein for a period sufficient to provide the desired effect.

5 The following examples further describe and demonstrate preferred embodiments within the scope of the present invention. The examples are given solely for the purposes of illustration and are not to be construed as illustrative of limitations of this invention. Many variations thereof are possible without departing from the invention's spirit and scope.

EXAMPLES 1-4

The following compositions/capsules are representative of the present invention.

<u>Component</u>	<u>Weight %</u>			
Gelatin	12.578	12.328	12.578	17.578
Sorbitol Solution (70% Aqueous)	2.046	2.05	2.046	2.046
Saccharin	0.372	0.500	0.372	0.450
FD&C Blue #1	0.002	0.002	0.002	-
FD&C Yellow #5	0.002	-	0.002	0.004
Captex 300 <sup>1</sup>	72.140	70.00	71.925	66.142
Flavor	12.750	15.00	12.75	13.500
Cetyl Pyridinium Chloride	0.100	-	-	-
Domiphen Bromide	0.010	-	-	-
Chlorhexidine	-	0.12	-	-
ZnCl <sub>2</sub>	-	-	0.025	-
Sodium Lauryl Sulfate	-	-	0.300	-
Triclosan	-	-	-	0.28

1) Captex 300 is a triglyceride supplied by Capitol City Product, Columbus, Ohio.

35 The above compositions are prepared by mixing the components of the core in one container and the components of the shell in another container. The shell materials are heated to provide a fluid medium. The core and shell materials are then pumped

separately to a two-fluid nozzle submerged in an organic carrier medium. The capsules formed are allowed to cool and stiffen. They are then denatured and separated for further handling.

In the above compositions any of a wide variety of other shell materials, breath control agents, sweeteners as well as other components may be used in place of or in combination with the components listed above.

WHAT IS CLAIMED IS:

1. Microcapsules suitable for reducing oral bacteria and providing breath protection comprising a shell material suitable for use in the mouth and ingesting and a core composition comprising a breath protection agent/anti-microbial selected from the group consisting of quaternary ammonium salts, other cationic salts, copper salts, zinc salts, triclosan and mixtures thereof and an organic diluent.
2. Microcapsules according to Claim 1 wherein the shell material is selected from the group consisting of polyvinyl alcohol, gelatin, waxes, gums and sugar candies.
3. Microcapsules according to either of Claims 1 or 2 wherein the microcapsule is in the form of a sphere, oblong, disk, a puffed square, or a cylinder and the breath control agent is a quaternary ammonium salt.
4. Microcapsules according to any of Claims 1-3 wherein the microcapsules are in the form of spheres.
5. Microcapsules according to Claim 4 wherein the microcapsules are from about 2mm to about 9mm in diameter and the shell wall thickness is from about 30um to about 2mm.
6. Microcapsules according to any of Claims 1-5 wherein the shell material is gelatin.
7. Use of a breath protection agent/antibacterial in the manufacture of microcapsules for reducing oral bacteria and breath odor in the mouth wherein the microcapsules comprise a shell material suitable for use in the mouth and ingesting and a core composition comprising a breath protection



agent/antimicrobial selected from the group consisting of quaternary ammonium salts, other cationic salts, copper salts, zinc salts, triclosan and mixtures thereof and an organic diluent.

8. A manufacture according to Claim 7 wherein the microcapsule shell is made of gelatin.
9. A manufacture according to either of Claims 7 or 8 wherein the breath control/antimicrobial active is selected from the group consisting of cetyl pyridinium chloride, domiphen bromide and mixtures thereof.
10. A method according to any of Claims 7-9 wherein the microcapsule is in the form of a sphere.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 92/10500

## A. CLASSIFICATION OF SUBJECT MATTER

IPC5: A61K 9/50, A61K 7/16

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC5: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG: WPI, WPIL, CLAIMS, MEDLINE, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO, A1, 8100205 (ARTHUR BARR), 5 February 1981 (05.02.81) --	1-10
Y	WO, A1, 9015592 (PATRICK JOHN SHANAHAN), 27 December 1990 (27.12.90) --	1-10
Y	EP, A1, 0485616 (SUNSTAR KABUSHIKI KAISHA), 20 May 1992 (20.05.92), see page 2 lines 1-40 --	1-10

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 92/10500

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>Dialog Information Services, World Patent Index - latest, File 351, Dialog accession no. 007957913, WPI Acc No: 89-223025/31, ((LIOY) LION CORP), "Compsn. for mouth, e.g. tooth paste - contg. copper cpds. selected from copper gluconate and its alkali metal salt and copper citrate, chlorhexidine gluconate etc.", JP 1153620, A, 890615, 8931</p> <p style="text-align: center;">--</p>	1-8,10
Y	<p>US, A, 5043154 (ABDUL GAFFAR ET AL.), 27 August 1991 (27.08.91)</p> <p style="text-align: center;">--</p> <p style="text-align: center;">-----</p>	1-8,10

**INTERNATIONAL SEARCH REPORT**  
 Information on patent family members

26/02/93

International application No.

PCT/US 92/10500

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